#### PATENT COOPERATION TREATY

## **PCT**

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER		see Form PCT/ISA/220			
CEL63169PC/mo	ACTION	as well	ell as, where applicable, item 5 below.			
International application No.	International filing date (day/month	/year)	(Earliest) Priority Date (day/month/year)			
PCT/EP2004/013538	29/11/2004	29/11/2004 29/01/2004				
Applicant						
CELLZOME AG						
This International Search Report has beer according to Article 18. A copy is being tra	n prepared by this International Search Insmitted to the International Bureau	ching Auth	ority and is transmitted to the applicant			
This International Search Report consists	of a total of she	ets.	•			
X It is also accompanied by	a copy of each prior art document cit	ed in this	report.			
	on a military manager and early list le	m.				
The international s this Authority (Rule	earch was carried out on the basis on the basis on the basis on the basis of 23.1(b)).	f a transla	tion of the international application furnished to			
b. X With regard to any nucleo	tide and/or amino acid sequence (	lisclosed i	n the international application, see Box No. I.			
2. X Certain claims were found unsearchable (See Box II).						
3. Unity of invention is lack	ing (see Box III).					
4. With regard to the title,						
the text is approved as sub	mitted by the applicant.		·			
X the text has been establish	ed by this Authority to read as follow	s:				
TREATMENT OF NEURODEGEN			OF ATP7A-MODULATORS			
	,					
5. With regard to the abstract,			·			
X the text is approved as sub	mitted by the applicant.					
the text has been established may, within one month from	ed, according to Rule 38.2(b), by this the date of mailing of this internation	Authority nal search	as it appears in Box No. IV. The applicant report, submit comments to this Authority.			
6. With regard to the drawings,						
a. the figure of the drawings to be published with the abstract is Figure No						
as suggested by the						
as selected by this	Authority, because the applicant faile	d to sugge	est a figure.			
as selected by this A	Authority, because this figure better of	haracteriz	tes the invention.			
b. X none of the figures is to be p	published with the abstract.		1			

#### INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2004/013538

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet) With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of: type of material a. a sequence listing table(s) related to the sequence listing format of material in written format Х in computer readable form time of filing/furnishing contained in the international application as filed filed together with the international application in computer readable form furnished subsequently to this Authority for the purpose of search 2. Χ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished. 3. Additional comments:

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N9/14 C12N15/11

A61K31/713 C12Q1/34

According to International Patent Classification (IPC) or to both national classification and IPC

#### **B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols) C12N A61K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, WPI Data, PAJ, Sequence Search

Category °	Citation of document with indication	· · · · · · · · · · · · · · · · · · ·
	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	BAYER THOMAS A ET AL: "Dietary Cu stabilizes brain superoxide dismutase 1 activity and reduces amyloid Abeta production in APP23 transgenic mice." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 100, no. 24, 25 November 2003 (2003-11-25), pages 14187-14192, XP002339932 ISSN: 0027-8424 the whole document	1,6,13, 15,16
	<b>-/</b>	
	;	

χ Further documents are listed in the continuation of box C. χ Patent family members are listed in annex.					
Special categories of cited documents :					
"A" document defining the general state of the art which is not considered to be of particular relevance  "E" earlier document but published on or after the international filling date  "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  "O" document referring to an oral disclosure, use, exhibition or other means  "P" document published prior to the international filing date but later than the priority date claimed	<ul> <li>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention.</li> <li>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone.</li> <li>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</li> <li>"&amp;" document member of the same patent family</li> </ul>				
Date of the actual completion of the international search	Date of mailing of the international search report				
10 August 2005	22/08/2005				
Name and mailing address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2  NL - 2280 HV Rijswijk  Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,	Authorized officer				
Fax: (+31-70) 340-2040, 1x. 31 651 epo ni,	Andres, S				

### PCT/EP2004/013538

Category °	ation) DOCUMENTS CONSIDERED TO BE RELEVANT  Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Jakegory	oralism of cocomoni, with microcaphiophiate, of the relevant passages	Relevant to claim No.
A	WAGGONER D J ET AL: "The role of copper in neurodegenerative disease." NEUROBIOLOGY OF DISEASE, vol. 6, no. 4, August 1999 (1999-08), pages 221-230, XP002339933 ISSN: 0969-9961 page 226 - page 227	1-6
A	CHERNY R A ET AL: "TREATMENT WITH A COPPER-ZINC CHELATOR MARKEDLY AND RAPIDLY INHIBITS BETA-AMYLOID ACCUMULATION IN ALZHEIMER'S DISEASE TRANSGENIC MICE" NEURON, vol. 30, no. 3, June 2001 (2001-06), pages 665-676, XP001034969 the whole document	1-6
A	WO 98/15828 A (SCIOS INC; CORDELL, BARBARA; HIGAKI, JEFFREY, N) 16 April 1998 (1998-04-16) the whole document	7-11
А	WO 01/16355 A (BOEHRINGER INGELHEIM PHARMA KG; FECHTELER, KATJA; FUCHS, KLAUS; KOSTKA) 8 March 2001 (2001-03-08) the whole document	7-11
A	VOSKOBOINIK ILIA ET AL: "The regulation of catalytic activity of the Menkes copper-translocating P-type ATPase: Role of high affinity copper-binding sites" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 276, no. 30, 27 July 2001 (2001-07-27), pages 28620-28627, XP002339934 ISSN: 0021-9258	
A	HOPF C ET AL: "Discovery of new therapeutic targets by integrated protein pathway and chemical proteomic analysis of APP processing" SOCIETY FOR NEUROSCIENCE ABSTRACTS, vol. 2003, 10 November 2003 (2003-11-10), page 1, XP002292236 ISSN: 0190-5295	

#### 10/24/76

# IAP11 Rec'd PCT/PTO 26 JUL 2006

International Application No. PCT/EP2004 /013538

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claim 16 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.2

Claims Nos.: 11,12,14

Present claims relate to compounds defined by reference to a desirable characteristic or property, namely their capacity to interact with ATP7A and/or with gamma-secretase and/or beta-secretase. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of claims 1-6,13 and 15-17 which appear to be clear, supported and disclosed, namely those parts relating to the siRNAs as described in example 2. Concerning claims 11, 12 and 14 no meaningful search could be done.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

#### INTERNATIONAL SEARCH REPORT

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)				
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:				
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  Although claim 16 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.				
2. X Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  see FURTHER INFORMATION sheet PCT/ISA/210				
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).				
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)				
This International Searching Authority found multiple inventions in this international application, as follows:				
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.				
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.				
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:				
No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:				
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.				

#### Information on patent family members

International Application No PCT/EP2004/013538

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 9815828	Α	16-04-1998	AU WO	4589297 9815828		05-05-1998 16-04-1998
WO 0116355	A	08-03-2001	DE CA WO EP JP MX	19941039 2381952 0116355 1212454 2003508058 PA02001754	A1 A2 A2 T	01-03-2001 08-03-2001 08-03-2001 12-06-2002 04-03-2003 23-10-2002